2017 ESC Pocket Guidelines

Committee for Practice Guidelines

PAD

2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases

ESC
European Society of Cardiology

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Introduction

The term “peripheral arterial diseases” (PADs) encompasses all arterial diseases other than coronary arteries and the aorta. This should be clearly distinguished from the term “peripheral artery disease” often used to name lower extremity artery disease (LEAD). Indeed, other peripheral localizations (Figure 1) are also frequently affected, mainly by atherosclerosis, and complete the family of PADs.

Because of multiple presentations and therapeutic options, a multidisciplinary management of these patients is mostly necessary, and cardiologists should be sensitive in regard to the diagnosis and management of patients with PADs, as many of them are seen and managed for concomitant cardiac conditions. Major efforts are still necessary to sensitize healthcare providers, decision makers and the general population about the need for awareness, screening, prevention and management of the 40 million individuals in our continent affected by PADs.

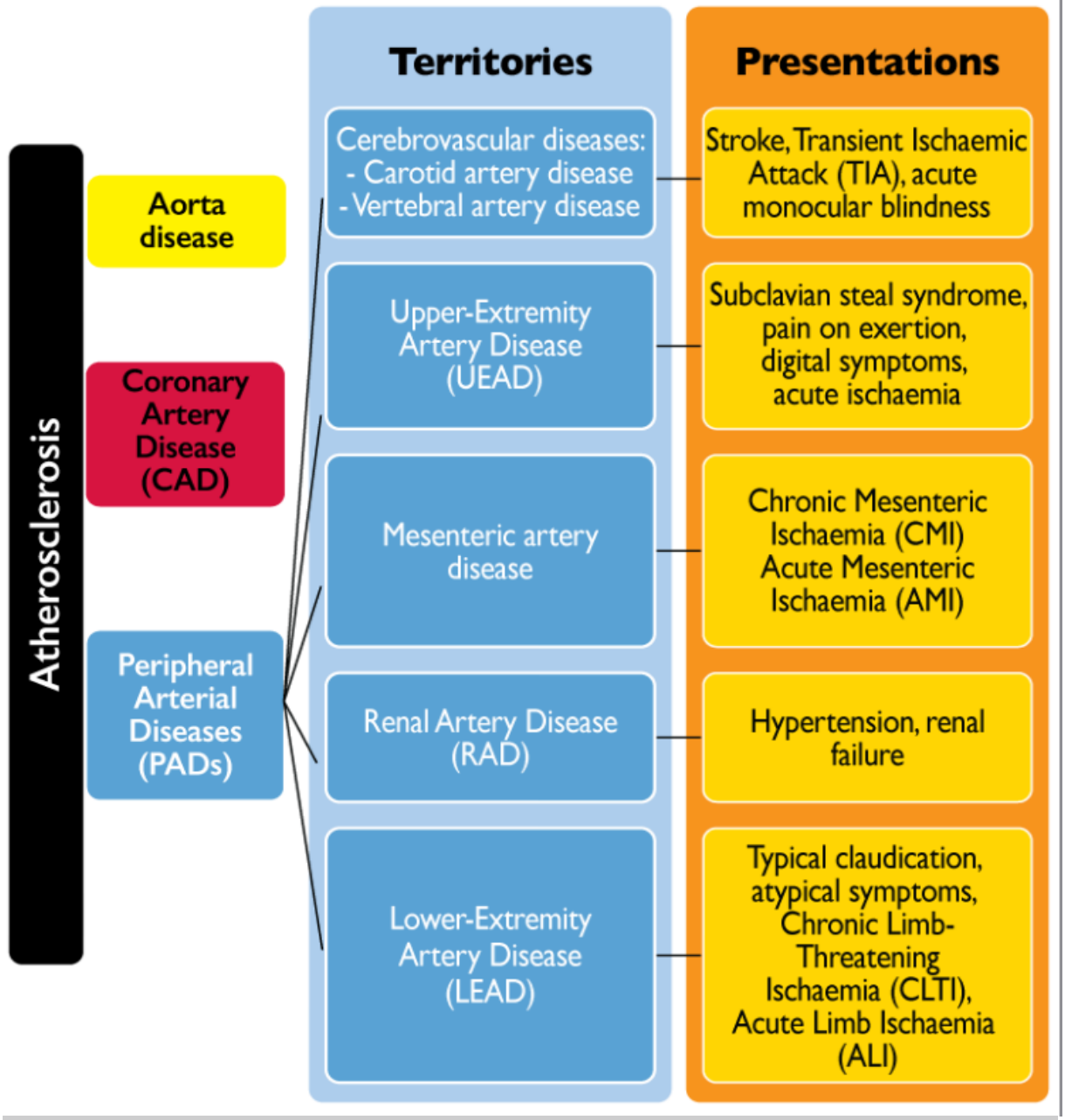
General recommendations on the management of patients with peripheral arterial diseases

Recommendations	Class[a]	Level[b]
In healthcare centres, it is recommended to set up a multidisciplinary Vascular Team to make decisions for the management of patients with PADs.	I	C
It is recommended to implement and support initiatives to improve medical and public awareness of PADs, especially cerebrovascular and lower extremity artery diseases.	I	C

Epidemiology and risk factors

The risk of different localizations of PADs increases with age and with exposure to major CV risk factors: smoking, hypertension, dyslipidaemia and diabetes. The strength of association between each risk factor and each vascular territory is variable. When a vascular territory is affected by atherosclerosis, not only is the corresponding organ endangered (e.g. the brain for carotid artery disease) but also the total risk of any cardiovascular event is increased (e.g. coronary events).

Figure 1 Presentations of Peripheral Arterial Diseases (PADs)



Overview

Thorough clinical history and physical examination are key steps in PADs management (Tables 1 & 2).

Laboratory testing (Table 3) is a key component especially for assessing the risk factors and end organ damages.

The Ankle-Brachial Index (ABI) has a specific particularity since it can not only diagnose LEAD but can be used as marker of atherosclerosis and risk of mortality and CV events (Table 4).

Table 1 Main points of medical history for assessment of peripheral arterial diseases

Family history of CVD (coronary artery disease, cerebrovascular disease, aortic aneurysm, LEAD), and premature CVD (fatal or non-fatal CVD event or/and established diagnosis of CVD in first degree male relatives before 55 years or female relatives before 65 years).
Personal history of: • Hypertension • Diabetes • Dyslipidaemia • Smoking (present and/or past), passive smoking exposure • Prior CVD • Chronic kidney disease • Sedentary life • Dietary habits • History of cancer radiation therapy • Psycho-social factors
Transient or permanent neurological symptoms.
Arm exertion pain, particularly if associated with dizziness or vertigo.
Symptoms suggesting angina, dyspnoea.
Abdominal pain, particularly if related to eating and associated with weight loss.
Walking impairment/claudication: • type: fatigue, aching, cramping, discomfort, burning • location: buttock, thigh, calf, or foot • timing: triggered by exercise, uphill rather than downhill, quickly relieved with rest; chronic • distance
Lower limb pain (including foot) at rest, and evolution at upright or recumbent position.
Poorly healing wounds of the extremities.
Physical activity assessment: • Functional capacity and causes of impairment.
Erectile dysfunction.

CVD = cardiovascular disease; LEAD = lower extremity artery disease.

Table 2 Physical examination for assessment of peripheral arterial diseases

Auscultation and palpation of cervical and supraclavicular areas.
Careful inspection of upper extremities, including hands (i.e. colour, skin integrity).
Palpation of upper extremity pulses.
Blood pressure measurement of both arms and notation of inter-arm difference.
Auscultation at different levels including the flanks, peri-umbilical region, and groin.
Abdominal palpation, palpation of femoral, popliteal, dorsalis pedis, and posterior tibial artery pulses, temperature gradient assessment.
Careful inspection of lower limbs, including feet (i.e. colour, presence of any cutaneous lesion). Findings suggestive of lower extremity arterial disease, including calf hair loss and muscle atrophy, should be noted.
Peripheral neuropathy assessment in case of diabetes or LEAD: sensory loss (monofilament testing), ability to detect pain and light touch (sharp examination pin, cotton wool), vibration impairment (128 Hz tuning fork); deep tendon reflexes examination; sweating.

Table 3 Laboratory testing in patients with peripheral arterial diseases

Routine tests
Fasting plasma glucose.
Fasting serum lipid profile: • total cholesterol • triglycerides • high-density lipoprotein cholesterol • low-density lipoprotein cholesterol
Serum creatinine and creatinine clearance.
Urine analysis: urinary protein by dipstick test, microalbuminuria.
• Blood count • Uric acid
Additional tests, based on findings from clinical history, physical examination and routine tests
Either glycated haemoglobin if fasting plasma glucose >5.6 mmol/L (101 mg/dL) or impaired glucose tolerance test when there is doubt.
Lipoprotein(a) if there is a family history of premature cardiovascular disease.
Quantitative proteinuria if positive dipstick test.

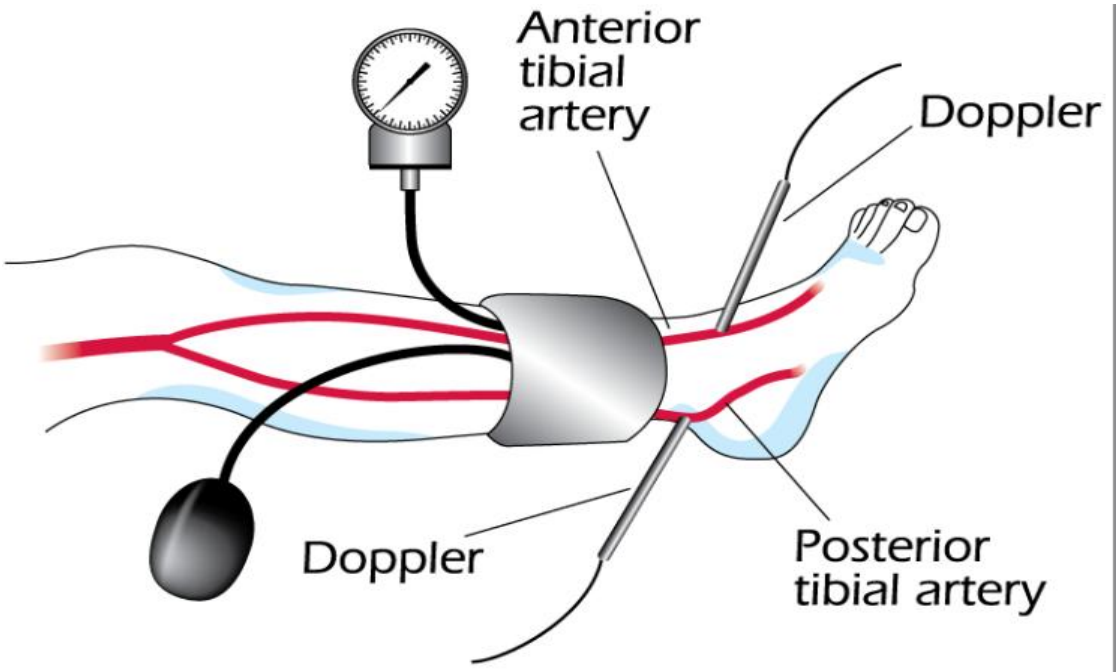
Table 4 The Ankle-Brachial Index

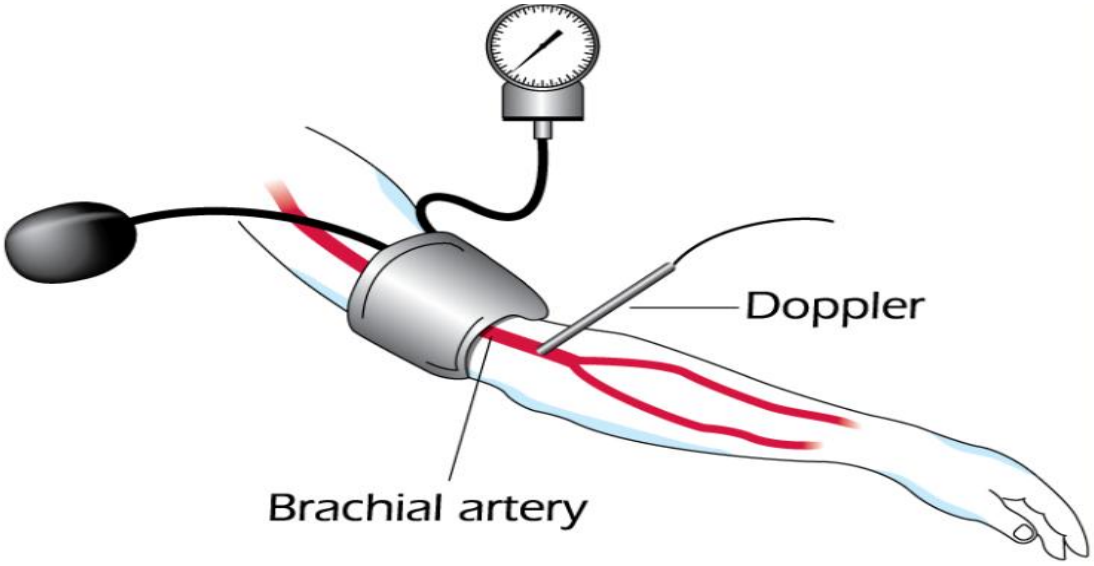
1. Who should have an ABI measurement in clinical practice?

- **Patients with clinical suspicion for LEAD:**
  - Lower extremities pulse abolition and/or arterial bruit
  - Typical intermittent claudication or symptoms suggestive for LEAD
  - Non-healing lower extremity wound
- **Patients at risk for LEAD because of the following clinical conditions:**
  - Atherosclerotic diseases: CAD, any PADs
  - Other conditions: AAA, CKD, heart failure
- **Asymptomatic individuals clinically-free but at-risk for LEAD:**
  - Men and women aged >65 years
  - Men and women aged <65 years classified at high CV risk according the ESC Guidelines[a]
  - Men and women aged >50 years with family history for LEAD

2. How to measure the ABI?

In supine position, with cuff placed just above the ankle, avoiding wounded zones. After a 5–10 minute rest, the SBP is measured by a Doppler probe (5–10 MHz) on the posterior and the anterior tibial (or dorsal pedis) arteries of each foot and on the brachial artery of each arm. Automated BP cuffs are mostly not valid for ankle pressure and may display overestimated results in case of low ankle pressure. The ABI of each leg is calculated by dividing the highest ankle SBP by the highest arm SBP.





3. How to interpret the ABI?

- For diagnosis of LEAD interpret each leg separately (one ABI per leg).
- For the CV risk stratification: take the lowest ABI between the two legs.
- Interpretation:

[a]Subjects with: markedly elevated single risk factors; diabetes mellitus (except for young people with type 1 diabetes without other major risk factors); a calculated SCORE ≥5% and <10%.

The management of patients with PADs includes both interventions to address specific arterial symptoms and general CV risk prevention. Best medical therapy includes CV risk factor management with non-pharmacological measures (i.e. smoking cessation, healthy diet, weight loss and regular physical exercise) and optimal pharmacological therapy.

Recommendations in patients with peripheral arterial diseases: best medical therapy

Recommendations	Class[a]	Level[b]
Smoking cessation is recommended in all patients with PADs.	I	B
Healthy diet and physical activity are recommended for all patients with PADs.	I	C
Statins are recommended in all patients with PADs.	I	A
In patients with PADs, it is recommended to reduce LDL-C to <1.8 mmol/L (70 mg/dL) or decrease it by ≥50% if baseline values are 1.8–3.5 mmol/L (70–135 mg/dL).	I	C
In diabetic patients with PADs, strict glycaemic control is recommended.	I	C
Antiplatelet therapy is recommended in patients with symptomatic PADs.	I	C[d]
In patients with PADs and hypertension, it is recommended to control blood pressure at <140/90 mmHg.	I	A
ACEIs or ARBs should be considered as first line therapy in patients with PADs and hypertension.[c]	IIa	B

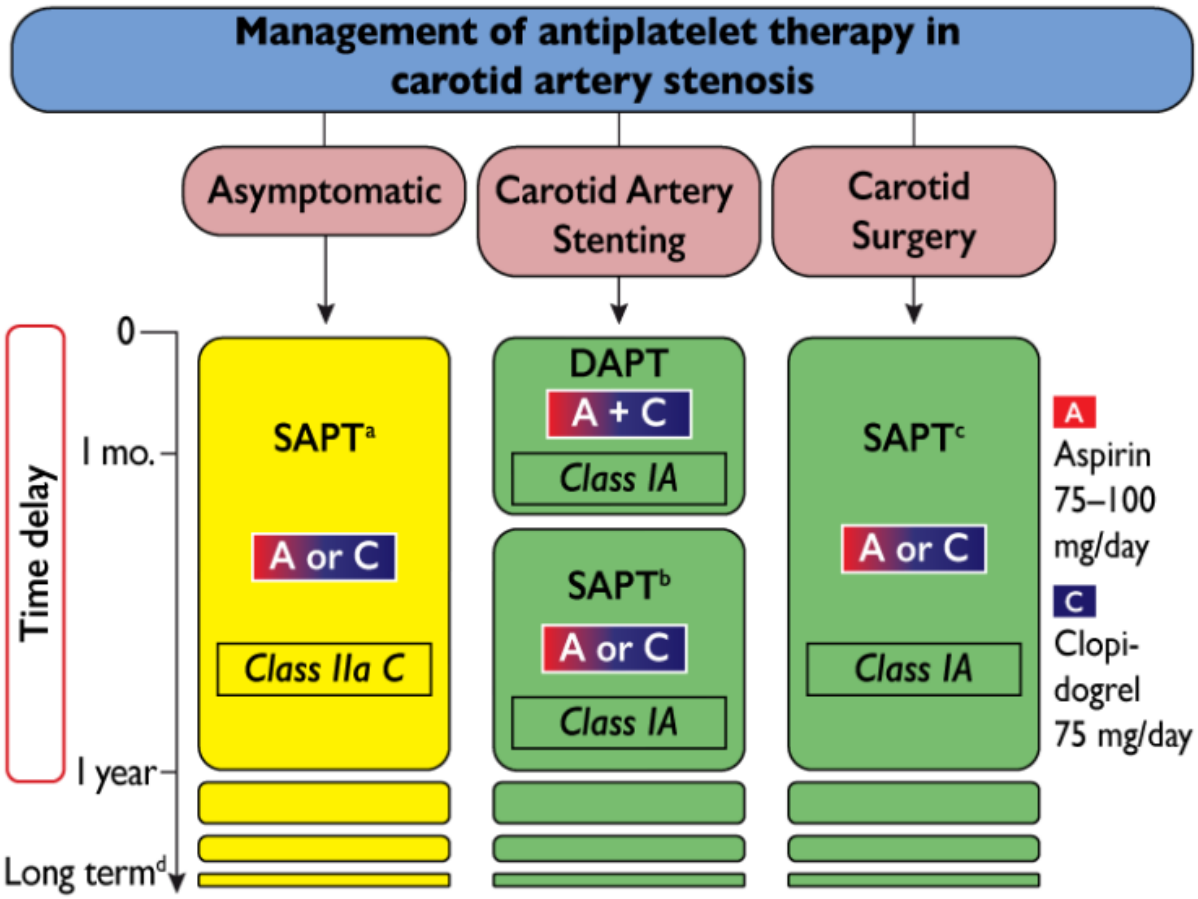
ACEIs = angiotensin-converting enzyme inhibitors; ARBs = angiotensin-receptor blockers; BP = blood pressure; HbA1c = glycated haemoglobin; LDL-C = low-density lipoprotein cholesterol; LEAD = lower extremity artery disease; PADs = peripheral arterial diseases.

[c]Calcium channel blockers should be proposed in black individuals.

[d]Evidence is not available for all sites.When evidence is available, recommendations specific for the vascular site are presented in the corresponding sections.

This chapter addresses specifically the antithrombotic therapy, as part of best medical therapy, in most frequent cases. Other cases with PADs (e.g. renal artery disease) without any specific indication for oral anticoagulation (e.g. atrial fibrillation) require long-term antiplatelet therapy.

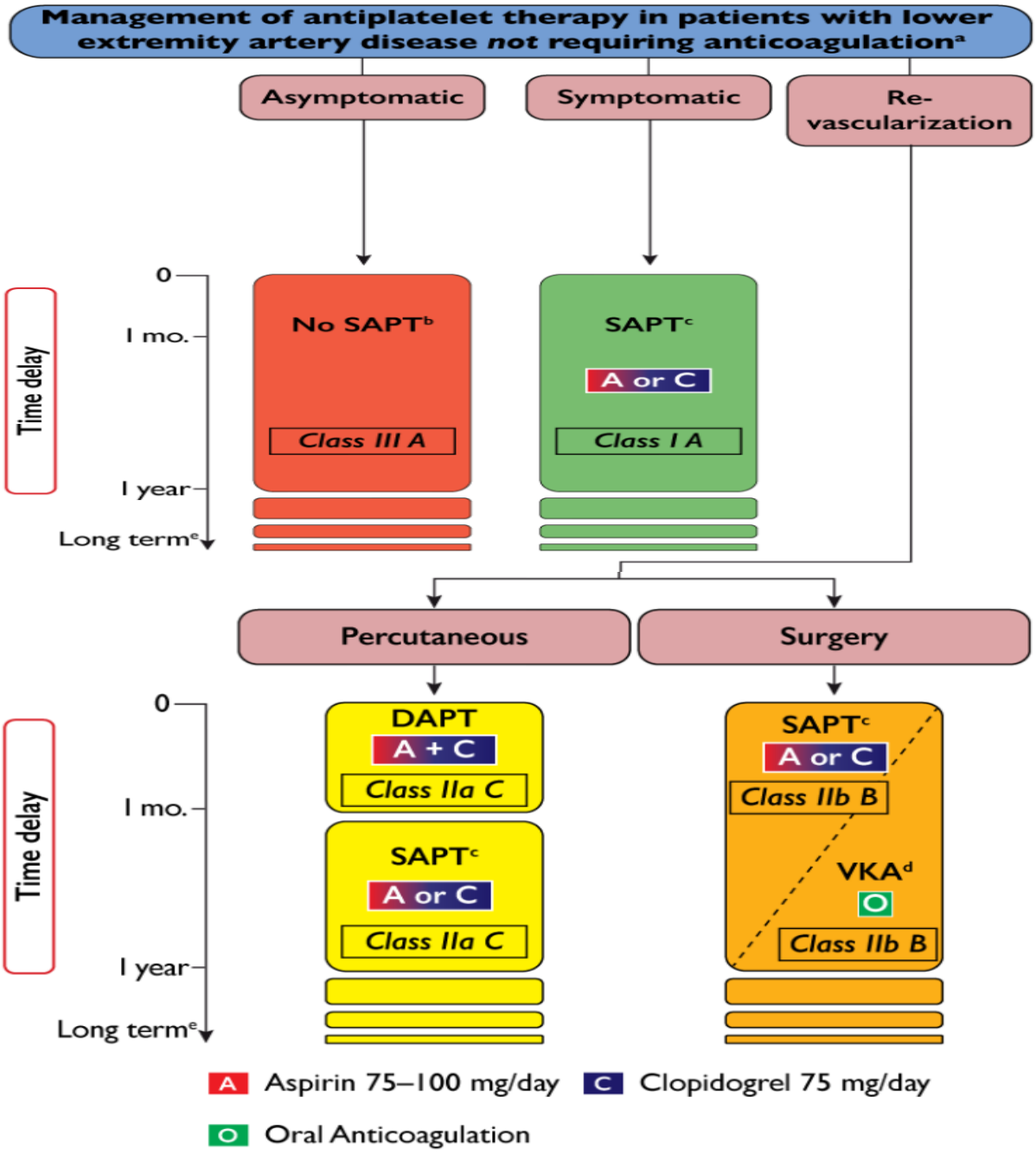
Figure 2 Management of antithrombotic treatment in patients with carotid artery stenosis



DAPT = dual antiplatelet therapy, a daily combination of aspirin (75–100 mg) and clopidogrel (75 mg); CAS = carotid artery stenting; SAPT = single antiplatelet therapy; TIA = transient ischaemic attack.

[a]At the exception of patient at very high bleeding risk - [b]DAPT may be used if another indication supersedes that of carotid artery stenting such as acute coronary syndrome or percutaneous coronary intervention of less than 1 year - [c] In case of recent minor stroke or TIA.A loading dose of aspirin (300 mg) and/or clopidogrel (300/600 mg) is recommended at the acute phase of stroke/TIA or during CAS - [d]Stands for as long as it is well tolerated.

Figure 3 Antiplatelet therapy in patients with lower extremity artery disease



DAPT = dual antiplatelet therapy; SAPT = single antiplatelet therapy;VKA = vitamin K antagonist.

[a]e.g. concomitant AF or mechanical valve prosthesis.

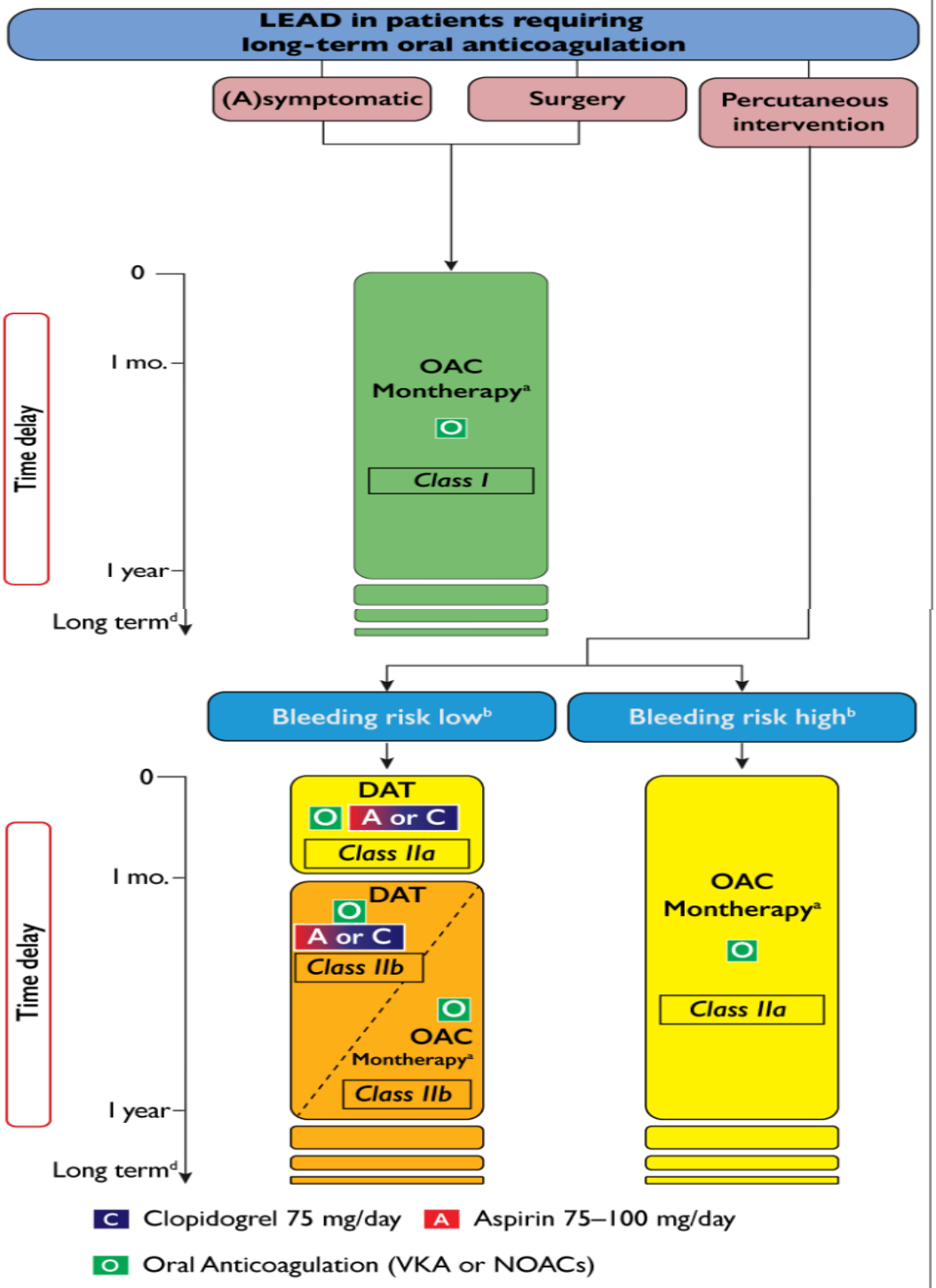
[b]SAPT should be considered if there is another concomitant atherosclerotic disease (e.g. coronary artery disease).

[c]DAPT may be considered in patients with recent acute coronary syndrome and/or percutaneous coronary intervention (<1 year), stenting of the last patent coronary artery, multiple coronary vessel disease in diabetic patients with incomplete revascularization.

[d]Evidence is weak and bleeding doubles as compared to SAPT.

[e]Stands for as long as it is well tolerated.

Figure 4 Antithrombotic therapy in patients with LEAD requiring oral anticoagulation



ACS = acute coronary syndrome; CAD = coronary artery disease; CLTI = chronic limb-threatening ischaemia; DAT = dual antithrombotic therapy;LEAD = lower extremity artery disease; OAC = oral anticoagulation.

[a]DAT may be considered in high ischaemic rick patients defined as prior stent thrombosis, acute limb ischaemia on OAC and concomitant CAD (recent ACS, stenting of the last patent coronary artery, multiple coronary vessel disease in diabetic patients with incomplete revascularization).

[b]Compared to the risk for stroke/CLTI due to stent/graft occlusion.

[c]Stands for as long as it is well tolerated.

Recommendations on antithrombotic therapy in patients with peripheral artery diseases

Recommendations	Class[a]	Level[b]
Carotid artery disease		
In patients with symptomatic carotid stenosis, long-term SAPT is recommended.	I	A
DAPT with aspirin and clopidogrel is recommended for at least one month after CAS.	I	B
In patients with asymptomatic >50% carotid artery stenosis, long-term antiplatelet therapy (commonly low dose aspirin) should be considered when the bleeding risk is low.[c]	IIa	C
Lower extremity artery disease		
Long-term SATP is recommended in symptomatic patients.	I	A
Long-term SATP is recommended in all patients who have undergone revascularization.	I	C
SATP is recommended after infra-inguinal bypass surgery.	I	A
In patients requiring antiplatelet therapy, clopidogrel may be preferred over aspirin.	IIb	B
Vitamin K antagonists may be considered after autologous vein infra- inguinal bypass.	IIb	B
DAPT with aspirin and clopidogrel for at least one month should be considered after infra-inguinal stent implantation.	IIa	C
DAPT with aspirin and clopidogrel may be considered in below-knee bypass with prosthetic graft.	IIb	B
Because of a lack of proved benefit, antiplatelet therapy is not routinely indicated in patients with isolated[d] asymptomatic LEAD.	III	A

Antithrombotic therapy for PADs patients requiring oral anticoagulant		
In patients with PADs and AF, oral anticoagulation:		
• is recommended when CHA_2DS_2-VASc score ≥2	I	A
• should be considered in all other patients	IIa	B
In patients with PADs who have an indication for OAC (e.g.AF or mechanical prosthetic valve), oral anticoagulants alone should be considered.	IIa	B
After endovascular revascularization, aspirin or clopidogrel should be considered in addition to OAC for at least I month if the bleeding risk is low compared to the risk of stent/graft occlusion.	IIa	C
After endovascular revascularization, OAC alone should be considered if the bleeding risk is high compared to the risk of stent/graft occlusion.	IIa	C
OAC and SAPT may be considered beyond one month in high ischaemic risk patients or when there is another firm indication for long-term SAPT.	IIb	C

AF = atrial fibrillation; CAS = carotid artery stenting; DAPT = dual antiplatelet; LEAD = lower extremity artery disease; OAC = oral anticoagulation; PADs = peripheral arterial diseases; SAPT = single antiplatelet therapy.

CHA_2DS_2-VASc score is calculated as follows: Congestive heart failure history (1 point), Hypertension (1 point),Age >75 years (2 points), Diabetes mellitus (1 point), Stroke or TIA or arterial thromboembolic history (1 point),Vascular disease history (1 point), Age between 65 and 74 years (1 point), Sex category (1 point if female).

[a]Class of recommendation.

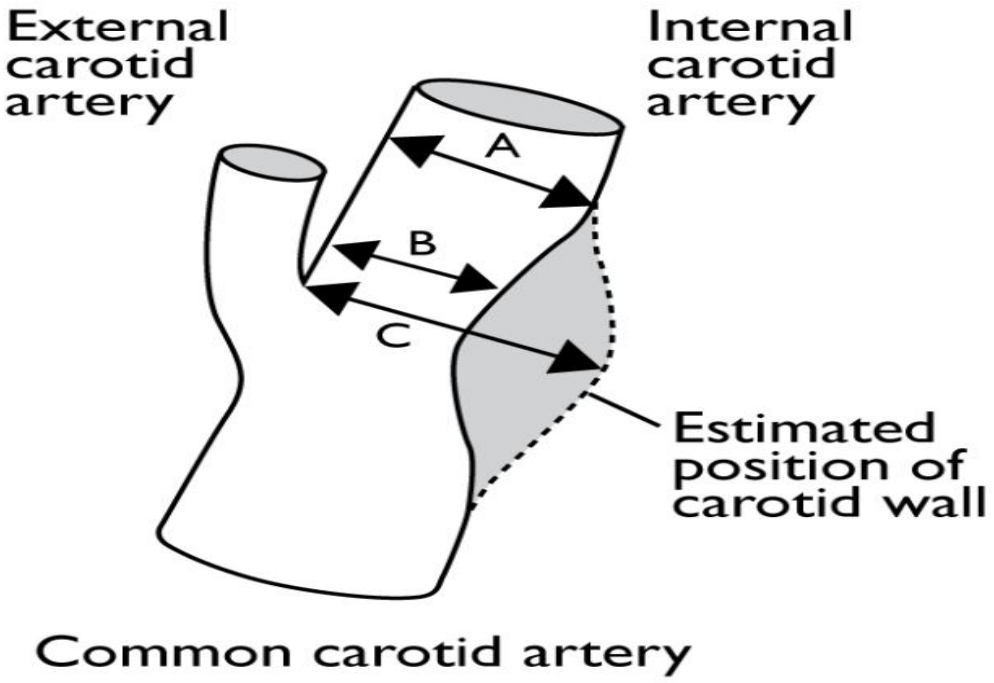
[b]Level of evidence.

[c]With the exception of patients with an indication for long-term oral anticoagulation.

[d]Without any other clinical cardiovascular condition requiring antiplatelet therapy (e.g. coronary artery disease or other multi-site artery diseases).

The management of carotid artery disease mostly depend on the symptomatic/asymptomatic characteristic, as well as the stenosis degree (Figure 4 and 5). Other characteristics can stratify the risk for patient with asymptomatic stenosis (Table 3).

Figure 5 Angiographic carotid stenosis according to different methods.



NASCET $\frac{A-B}{A}$	ECST $\frac{C-B}{C}$
NASCET	**ECST**
30	65
40	70
50	75
60	80
70	85
80	91
90	97

Approximate equivalent degrees of internal carotid artery stenosis used in NASCET and ESCT according to recent comparisons

ECST = European Carotid Surgery Trial; NASCET = North American Symptomatic Carotid Endarterectomy Trial

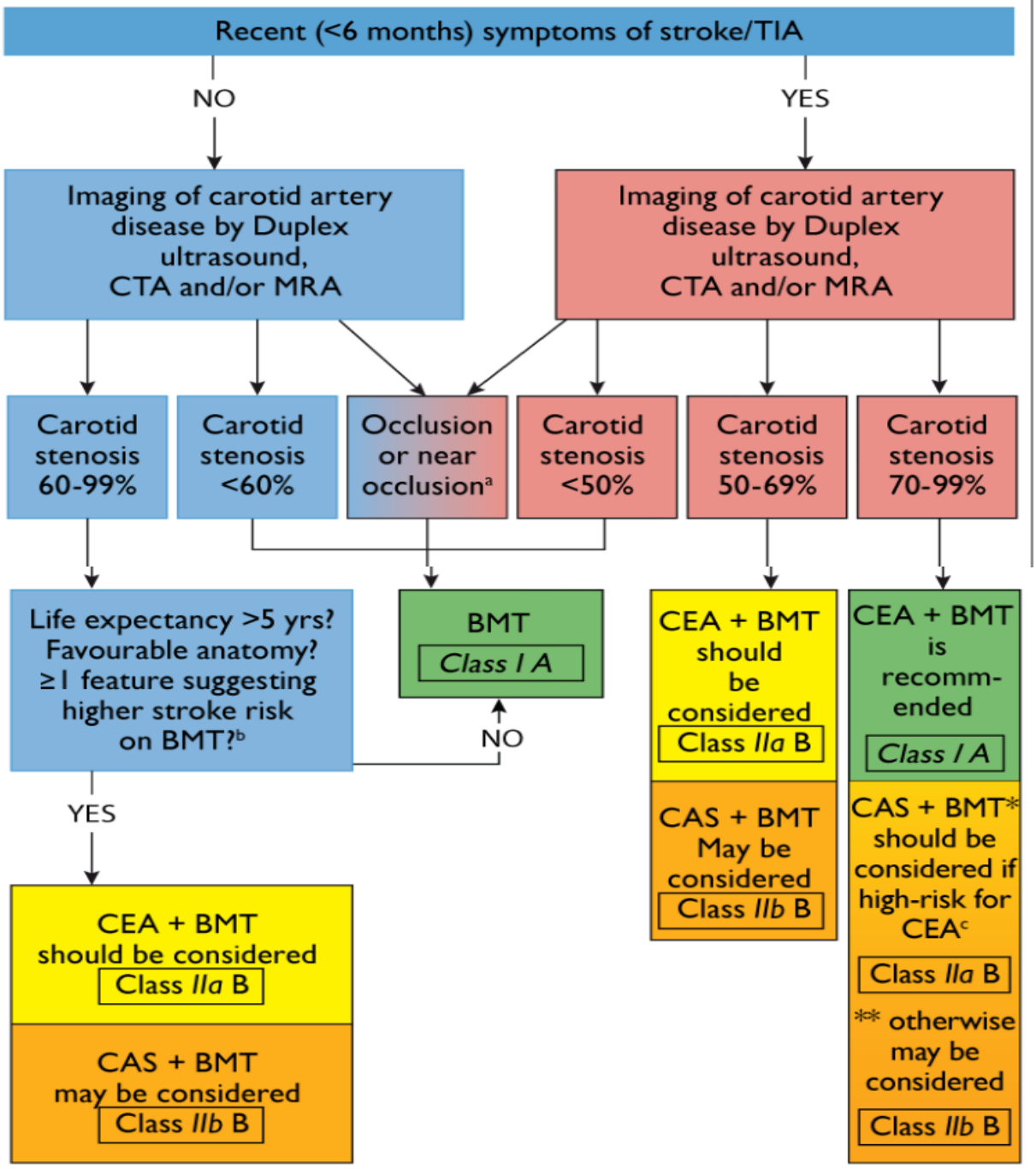
Recommendations for imaging of extracranial carotid arteries		
Recommendations	**Class[a]**	**Level[b]**
DUS (as first-line), CTA and/or MRA are recommended for evaluating the extent and severity of extracranial carotid stenoses.	I	B
When CAS is being considered, it is recommended that any DUS study be followed either by MRA or CTA to evaluate the aortic arch, as well as the extra- and intracranial circulation.	I	B
When CEA is considered, it is recommended that the DUS stenosis estimation be corroborated either by MRA or CTA (or by a repeat DUS study performed in an expert vascular laboratory).	I	B

CAS = carotid artery stenting; CEA = carotid endarterectomy; CTA = computed tomography angiography; DUS = duplex ultrasound; MRA = magnetic resonance an-

Recommendations for management of asymptomatic carotid artery disease		
Recommendations	**Class[a]**	**Level[b]**
In "average surgical risk" patients with an asymptomatic 60–99% stenosis, CEA should be considered in the presence of clinical and/or more imaging characteristics[c] that may be associated with an increased risk of late ipsilateral stroke, provided documented perioperative stroke/death rates are <3% and the patient's life expectancy is >5 years.	IIa	B
In asymptomatic patients who have been deemed "high-risk for CEA"[d] and who have an asymptomatic 60–99% stenosis in the presence of clinical and/or imaging characteristics[c] that may be associated with an increased risk of late ipsilateral stroke, CAS should be considered, provided documented perioperative stroke/death rates are <3% and the patient's life expectancy is >5 years.	IIa	B
In "average surgical risk" patients with an asymptomatic 60–99% stenosis in the presence of clinical and/or imaging characteristics[d] that may be associated with an increased risk of late ipsilateral stroke, CAS may be an alternative to CEA provided documented perioperative stroke/death rates are <3% and the patient's life expectancy is >5 years.	IIb	B

BP = blood pressure; CAS = carotid artery stenting; CEA = carotid endarterectomy. [a]Class of recommendation - [b]Level of evidence. - [c]See Table 5 - [d]Age > 80 years, clinically significant cardiac disease, severe pulmonary disease, contralateral internal carotid artery occlusion, contralateral recurrent laryngeal nerve palsy, previous radical neck surgery or radiotherapy and recurrent stenosis after CEA.

Figure 6 Management of extracranial carotid artery disease



BMT = best medical therapy; CAS = carotid artery stenting; CEA = carotid endarterectomy; CTA = computed tomography angiography; MRA = magnetic resonance angiography;TIA = transient ischaemic attack.

[a]With post-stenotic internal carotid artery narrowed to the point of near occlusion -
[b]See Table 5.

[c]Age >80 years, clinically significant cardiac disease, severe pulmonary disease, contralateral internal carotid artery occlusion, contralateral recurrent laryngeal nerve palsy, previous radical neck surgery or radiotherapy and recurrent stenosis after CEA.

Table 5 Features associated with increased risk of stroke in patients with asymptomatic carotid stenosis treated medically (for details see Web Table 5, see Web Addenda online*)	
Clinical[a]	• Contralateral TIA/stroke
Cerebral imaging	• Ipsilateral silent infarction
Ultrasound imaging	• Stenosis progression (> 20%) • Spontaneous embolization on transcranial Doppler (HITS) • Impaired cerebral vascular reserve • Large plaques[b] • Echolucent plaques • Increased juxta-luminal black (hypoechogenic) area
MRA	• Intraplaque haemorrhage • Lipid-rich necrotic core

HITS = high intensity transient signal; MRA = magnetic resonance angiography; TIA = transient ischaemic attack.
[a]Age is not a predictor of poorer outcome -[b]More than 40 mm^2 on digital analysis.

Recommendations on revascularization in patients with symptomatic carotid disease[c]		
Recommendations	**Class[a]**	**Level[b]**
CEA is recommended in symptomatic patients with 70–99% carotid stenoses, provided the documented procedural death/stroke rate is <6%.	I	A
CEA should be considered in symptomatic patients with 50–69% carotid stenoses, provided the documented procedural death/stroke rate is <6%.	IIa	A
In recently symptomatic patients with a 50–99% stenosis who present with adverse anatomical features or medical comorbidities that are considered to make them "high-risk for CEA", CAS should be considered, provided the documented procedural death/stroke rate is <6%.	IIa	B
When revascularization is indicated in "average surgical risk" patients with symptomatic carotid disease, CAS may be considered as an alternative to surgery, provided the documented procedural death/ stroke rate is <6%.	IIb	B
When decided, it is recommended to perform revascularization of symptomatic 50–99% carotid stenoses as soon as possible, preferably within 14 days of symptom onset.	I	A
Revascularization is not recommended in patients with a <50% carotid stenosis.	III	A

[a]Class of recommendation - [b]Level of evidence - [c]Stroke or TIA occuring within the 6 months.

Recommendation on the use of embolic protection device during carotid stenting		
Recommendations	**Class[a]**	**Level[b]**
The use of embolic protection devices should be considered in patients undergoing carotid artery stenting.	IIa	C

Recommendations for management of vertebral artery stenoses		
Recommendations	**Class[a]**	**Level[b]**
In patients with symptomatic extracranial vertebral artery stenoses, revascularization may be considered for lesions ≥50% in patients with recurrent ischaemic events, despite optimal medical management.	IIb	B
Revascularization of asymptomatic vertebral artery stenosis is not indicated, irrespective of the degree of severity.	III	C

Upper extremity artery disease (UEAD) due to atherosclerosis is mostly situated at the brachio-cephalic trunk, the subclavian and axillary arteries. Other aetiologies should be considered (Table 6). When suspected, it can be assessed by DUS, CTA or MRA.

Table 6 Differential diagnosis in upper limbs artery disease

Causes	Subclavian	Axillary	Brachial	Forearm	Hand
Atherosclerosis	•				
Thoracic outlet syndrome	•				
Giant cell arteritis	•				
Takayasu arteritis	•	•			
Radiation artery fibrosis	•	•			
Embolic		•	•	•	•
Fibromuscular dysplasia		•			•
Buerger's disease				•	•
Ergotism				•	•
Connective tissue disease				•	•
Cytotoxic drugs					•
Arterial drug injection					•
Diabetes mellitus					•
Myeloproliferative disorders					•
Hypercoagulative status					•

Cryoglobulins					•
Repetitive trauma					•
Vinyl chloride exposure					•
Iatrogenic lesions	•	•	•	•	•

Recommendations on the management of subclavian artery stenosis		
Recommendations	**Class[a]**	**Level[b]**
In symptomatic patients with subclavian artery stenosis/occlusion revascularization should be considered.	**IIa**	C
In symptomatic patients with a stenotic/occluded subclavian artery, both revascularization options (stenting or surgery) should be considered and discussed case by case according to the lesion characteristics and patient's risk.	**IIa**	C
In asymptomatic subclavian artery stenosis, revascularization:		
• should be considered in the case of proximal stenosis in patients undergoing CABG using the ipsilateral internal mammary artery.	**IIa**	C
• should be considered in the case of proximal stenosis in patients who already have the ipsilateral internal mammary artery grafted to coronary arteries with evidence of myocardial ischaemia.	**IIa**	C
• should be considered in the case of subclavian artery stenosis and ipsilateral arteriovenous fistula for dialysis.	**IIa**	C
• may be considered in the case of bilateral		

Mesenteric artery disease is underdiagnosed and highly lethal. The prerequisite of diagnosis is clinical suspicion, followed by imaging.

Acute mesenteric ischaemia is more often related to embolism than to thrombotic occlusion. Outcome is very time-sensitive, and dependent on clinical suspicion.

Recommendations on the management of acute mesenteric ischaemia

Recommendations	Class[a]	Level[b]
Diagnosis		
In patients with suspected acute mesenteric ischaemia, urgent CTA is recommended.	I	C
In patients with suspicion of acute mesenteric ischaemia,the measurement of D-dimer should be considered to rule out the diagnosis.	IIa	B
Treatment		
In patients with acute thrombotic occlusion of the superior mesenteric artery, endovascular therapy should be considered as first line therapy for revascularization.	IIa	B
In patients with acute embolic occlusion of the superior mesenteric artery, both endovascular and open surgery therapy should be considered.	IIa	B

The classical symptoms of CMI are postprandial abdominal pain, weight loss, diarrhoea or constipation, and food aversion.

Recommendations for management of chronic mesenteric artery disease

Recommendations	Class[a]	Level[b]
Diagnosis		
In patients with suspected CMI, DUS is recommended as the first line examination.	I	C
In patients with suspected CMI, occlusive disease of a single mesenteric artery makes the diagnosis unlikely, and a careful search for alternative causes should be considered.	IIa	C
Treatment		
In patients with symptomatic multivessel CMI, revascularization is recommended.	I	C
In patients with symptomatic multivessel CMI, it is not recommended to delay revascularization in order to improve the nutritional status.	III	C

CMI = chronic mesenteric ischaemia; DUS = duplex ultrasound.

Atherosclerotic renal artery disease (RAD) is the most common cause of "renovascular hypertension". The clinical situations raising suspicion for RAD are enlisted in Table 7.

Table 7 Clinical situations raising suspicion for renal artery disease

Onset of hypertension before the age of 30 years.
Onset of severe hypertension after the age of 55 years, when associated with CKD or heart failure.
Hypertension and abdominal bruit.
Rapid and persistent worsening of previously controlled hypertension.
Resistant hypertension (i.e. other secondary form unlikely and target not achieved despite four drug classes including a diuretic and a mineralocorticoid-receptor antagonist in appropriate doses).
Hypertensive crisis (i.e. acute renal failure, acute heart failure, hypertensive encephalopathy, or grade 3–4 retinopathy).
New azotaemia or worsening of renal function after treatment with RAAS blockers.
Unexplained atrophic kidney or discrepancy in kidney size, or unexplained renal failure.
Flash pulmonary oedema.

CKD = chronic kidney disease; RAAS = renin-angiotensin-aldosterone system.

Recommendations for diagnostic strategies for renal artery disease

Recommendations	Class[a]	Level[b]
DUS (as first-line), CTA[c] and MRA[d] are recommended imaging modalities to establish a diagnosis of RAD.	I	B
DSA may be considered to confirm a diagnosis of RAD when clinical suspicion is high and the results of non-invasive examinations are inconclusive.	IIb	C
Renal scintigraphy, plasma renin measurements before and after ACEI provocation, and vein renin measurements are not recommended for screening of atherosclerotic RAD.	III	C

ACEI = angiotensin-converting enzyme inhibitor; CTA = computed tomography angiography; DSA = digital subtraction angiography; DUS = duplex ultrasound; eGFR = estimated glomerular filtration rate; MRA = magnetic resonance angiography; RAD = renal artery disease.

[a]Class of recommendation - [b]Level of evidence - [c]When eGFR is ≥60 mL/min - [d]When eGFR is ≥30 mL/min.

Recommendations for treatment strategies for renal artery disease		
Recommendations	**Class[a]**	**Level[b]**
Medical therapy		
ACEIs/ARBs are recommended for treatment of hypertension associated with unilateral RAS.	I	B
Calcium channel blockers,beta-blockers and diuretics are recommended for treatment of hypertension associated with renal artery disease.	I	C
ACEIs/ARBs may be considered in bilateral severe RAS and in the case of stenosis in a single functioning kidney, if well-tolerated and under close monitoring.	IIb	B
Revascularization		
Routine revascularization is not recommended in RAS secondary to atherosclerosis.	III	A
In cases of hypertension and/or signs of renal impairment related to renal arterial fibromuscular dysplasia, balloon angioplasty with bailout stenting should be considered.	IIa	B
Balloon angioplasty, with or without stenting, may be considered in selected patients with RAS and unexplained recurrent congestive heart failure or sudden pulmonary oedema.	IIb	C
In the case of an indication for revascularization,surgical revascularization should be considered for patients with complex anatomy of the renal arteries, after a failed endovascular procedure, or during open aortic surgery.	IIa	B

ACEI(s) = angiotensin-converting enzyme inhibitor(s); ARB(s) = angiotensin-receptor blocker(s); RAS = renal artery stenosis.

Clinical presentation

Most patients with LEAD are asymptomatic. Walking capacity must be assessed to detect clinically "masked LEAD". Atypical symptoms are frequent. Even asymptomatic patients with LEAD are at high-risk of CV events and must benefit from most CV preventive strategies.

Table 8 Clinical stages of lower extremity artery disease

Fontaine classification		
Stage		Symptoms
I		Asymptomatic
II	IIa	Non-disabling intermittent claudication
	IIb	Disabling intermittent claudication
III		Ischaemic rest pain
IV		Ulceration or gangrene

Rutherford classification		
Grade	Category	Symptoms
0	0	Asymptomatic
I	1	Mild claudication
I	2	Moderate claudication
I	3	Severe claudication
II	4	Ischaemic rest pain
III	5	Minor tissue loss
III	6	Major tissue loss

Diagnostic tests

Recommendations for ankle-brachial index measurement

Recommendations	**Class[a]**	**Level[b]**
Measurement of the ABI is indicated as a first-line non-invasive test for screening and diagnosis of LEAD.	I	C
In the case of incompressible ankle arteries or ABI >1.40, alternative methods such as the toe-brachial index, Doppler waveform analysis or pulse volume recording are indicated.	I	C

ABI = ankle-brachial index; LEAD = lower extremity artery disease.
[a]Class of recommendation - [b]Level of evidence.

Recommendations on imaging in patients with lower extremity artery disease		
Recommendations	**Class[a]**	**Level[b]**
DUS is indicated as first-line imaging method to confirm LEAD lesions.	I	C
DUS and/or CTA and/or MRA are indicated for anatomical characterization of LEAD lesions and guidance for optimal revascularization strategy.	I	C
Data from an anatomical imaging test should always be analyzed in conjunction with symptoms and haemodynamic tests prior to treatment decision.	I	C
DUS screening for AAA should be considered.	IIa	C

AAA = abdominal aorta aneurysm; CTA = computed tomography angiography; DUS = duplex ultrasound; LEAD = lower extremity artery disease; MRA = magnetic resonance angiography.

Recommendations on revascularization of aorto-iliac occlusive lesions[c]		
Recommendations	**Class[a]**	**Level[b]**
An endovascular-first strategy is recommended for short (i.e. <5 cm) occlusive lesions.	I	C
In patients fit for surgery, aorto-(bi)femoral bypass should be considered in aorto-iliac occlusion(s).	IIa	B
An endovascular-first strategy should be considered in long and/or bilateral lesions in patients with severe comorbidities.	IIa	B
An endovascular-first strategy may be considered for aorto-iliac occlusive lesions, if done by an experienced team and if it does not compromise subsequent surgical options.	IIb	B
Primary stent implantation, rather than provisional stenting, should be considered.	IIa	B
Open surgery should be considered in fit patients with an aortic occlusion extending up to the renal arteries.	IIa	C
In the case of ilio-femoral occlusive lesions, a hybrid procedure combining iliac stenting and femoral endarterectomy or bypass should be considered.	IIa	C
Extra-anatomical bypass may be indicated only for patients with no other alternatives for revascularization.	IIb	C

[a]Class of recommendation - [b]Level of evidence - [c]These recommendations apply both for patients with intermittent claudication and severe chronic limb ischaemia.

Recommendations on revascularization of femoro-popliteal occlusive lesions[c]

Recommendations	Class[a]	Level[b]
An endovascular-first strategy is recommended in short (i.e. <25 cm) lesions.	I	C
Primary stent implantation should be considered in short (i.e. <25 cm) lesions.	IIa	A
Drug-eluting balloons may be considered in short (i.e. <25 cm) lesions.	IIb	A
Drug-eluting stents may be considered for short (i.e. <25 cm) lesions.	IIb	B
Drug-eluting balloons may be considered for the treatment of in-stent restenosis.	IIb	B
In patients who are not at high-risk for surgery, bypass surgery is indicated for long (i.e. ≥25 cm) superficial femoral artery lesions when an autologous vein is available and life expectancy is >2 years.	I	B
The autologous saphenous vein is the conduit of choice for femoro- popliteal bypass.	I	A
When above-knee bypass is indicated, in the absence of any autologous saphenous vein, the use of a prosthetic conduit should be considered	IIa	A
In patients unfit for surgery, endovascular therapy may be considered in long (i.e. ≥25 cm) femoro-popliteal lesions.	IIb	C

[a]Class of recommendation - [b]Level of evidence - [c]These recommendations apply both for patients with intermittent claudication and chronic limb-threatening ischaemia.

Recommendations on revascularization of infra-popliteal occlusive lesions

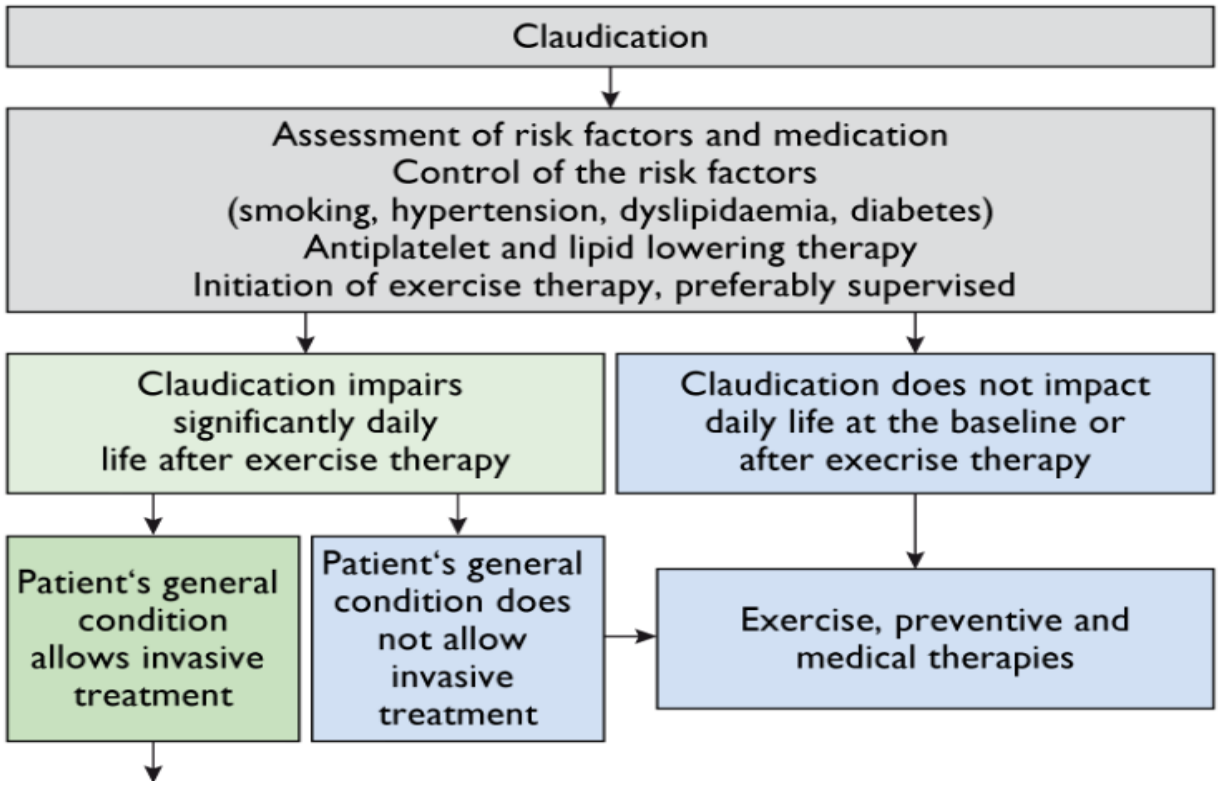
Recommendations	Class[a]	Level[b]
In the case of CLTI, infra-popliteal revascularization is indicated for limb salvage.	I	C
For revascularization of infra-popliteal arteries:		
• bypass using the great saphenous vein is indicated	I	A
• endovascular therapy should be considered.	IIa	B

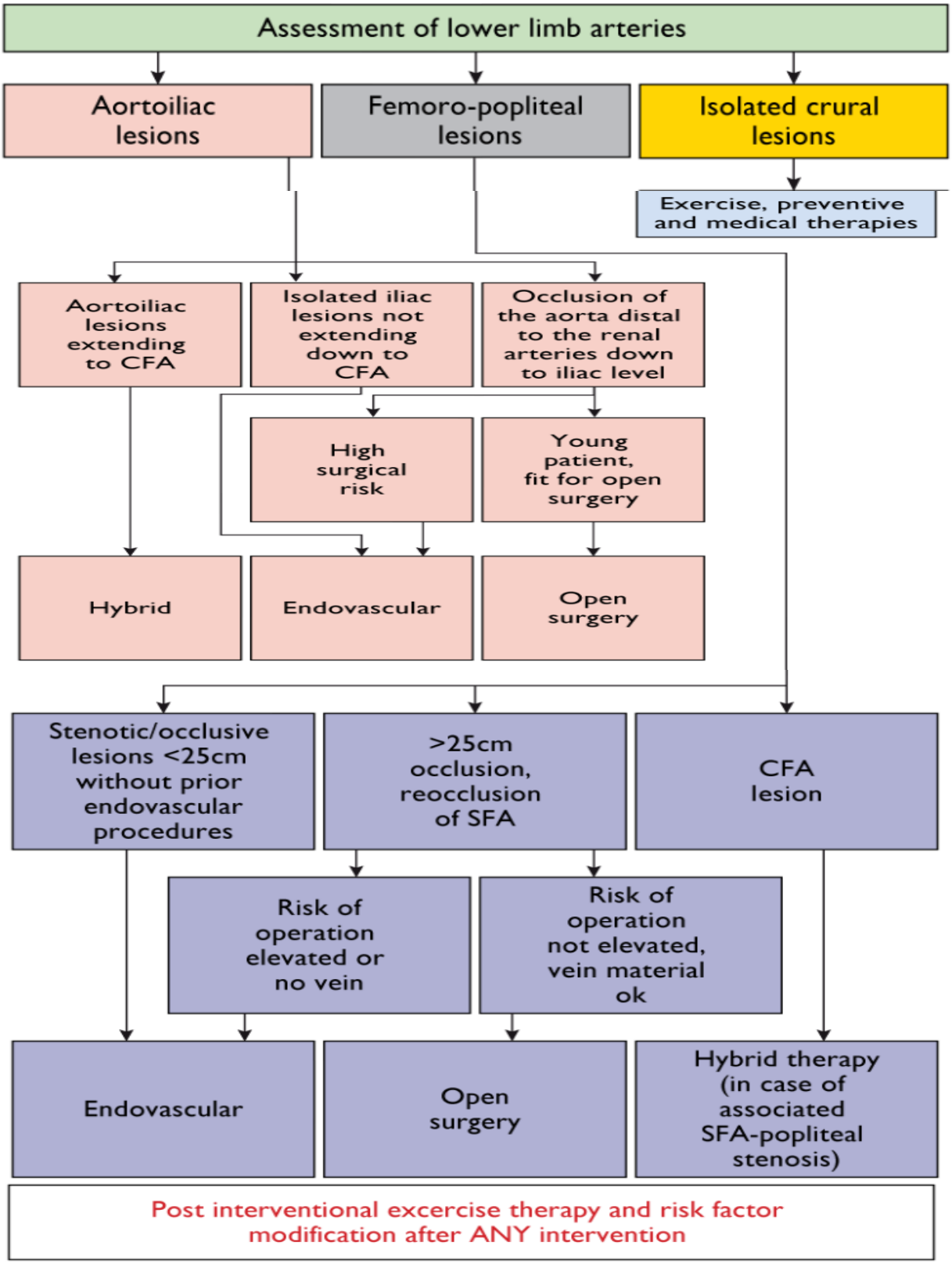
CLTI = chronic limb-threatening ischaemia. [a]Class of recommendation - [b]Level of evidence.

Recommendations for the management of patients with intermittent claudication

Recommendations	Class[a]	Level[b]
On top of general prevention, statins are indicated to improve walking distance.	I	A
In patients with intermittent claudication:		
• supervised exercise training is recommended.	I	A
• non-supervised exercise training is recommended when supervised exercise training is not feasible or available.	I	C
When daily life activities are compromised despite exercise therapy, revascularization should be considered.	IIa	C
When daily life activity is severely compromised, first line revascularization should be considered, in association with exercise therapy.	IIa	B

Figure 7 Management of patients with intermittent claudication[a]





CFA = common femoral artery; SFA = superficial femoral artery.
[a]Related to atherosclerotic lower extremity artery disease (LEAD).

CLTI specifies clinical patterns with vulnerable limb viability, related to ischaemia, wounds, and infection (Table 9 & Figure 8). Risk stratification and early recognition of tissue loss and/or infection and referral to the vascular specialist is mandatory for limb salvage by a multidisciplinary approach. Revascularization is indicated whenever feasible.

Table 9 Assessment of the risk of amputation: the WIFI classification

Score	Description		
W (Wound)			
0	No ulcer (ischaemic rest pain)		
1	Small, shallow ulcer on distal leg or foot without gangrene		
2	Deeper ulcer with exposed bone, joint or tendon ± gangrenous changes limited to toes		
3	Extensive deep ulcer, full thickness heel ulcer ± calcaneal involvement ± extensive gangrene		
I (Ischaemia)			
	ABI	Ankle pressure (mmHg)	Toe pressure or $TcPO_2$
0	≥0.80	>100	≥60
1	0.60–0.79	70–100	40–59
2	0.40–0.59	50–70	30–39
3	<0.40	<50	<30
fI (foot Infection)			
0	No symptoms/signs of infection		
1	Local infection involving only skin and subcutaneous tissue		
2	Local infection involving deeper than skin/subcutaneous tissue		
3	Systemic inflammatory response syndrome		

Example: A 65-year-old male diabetic patient with gangrene of the big toe and a <2 cm rim of cellulitis at the base of the toe, without any clinical/biological sign of general infection/inflammation, whose toe pressure is at 30 mmHg would be classified as Wound 2, Ischaemia 2, foot Infection 1 (WIfI 2-2-1).
The clinical stage would be 4 (high-risk of amputation). The benefit of revascularization (if feasible) is high, also depending on infection control.
[a]Adapted from Mills JL et al. J Vasc Surg 2014;59(1):220–234.

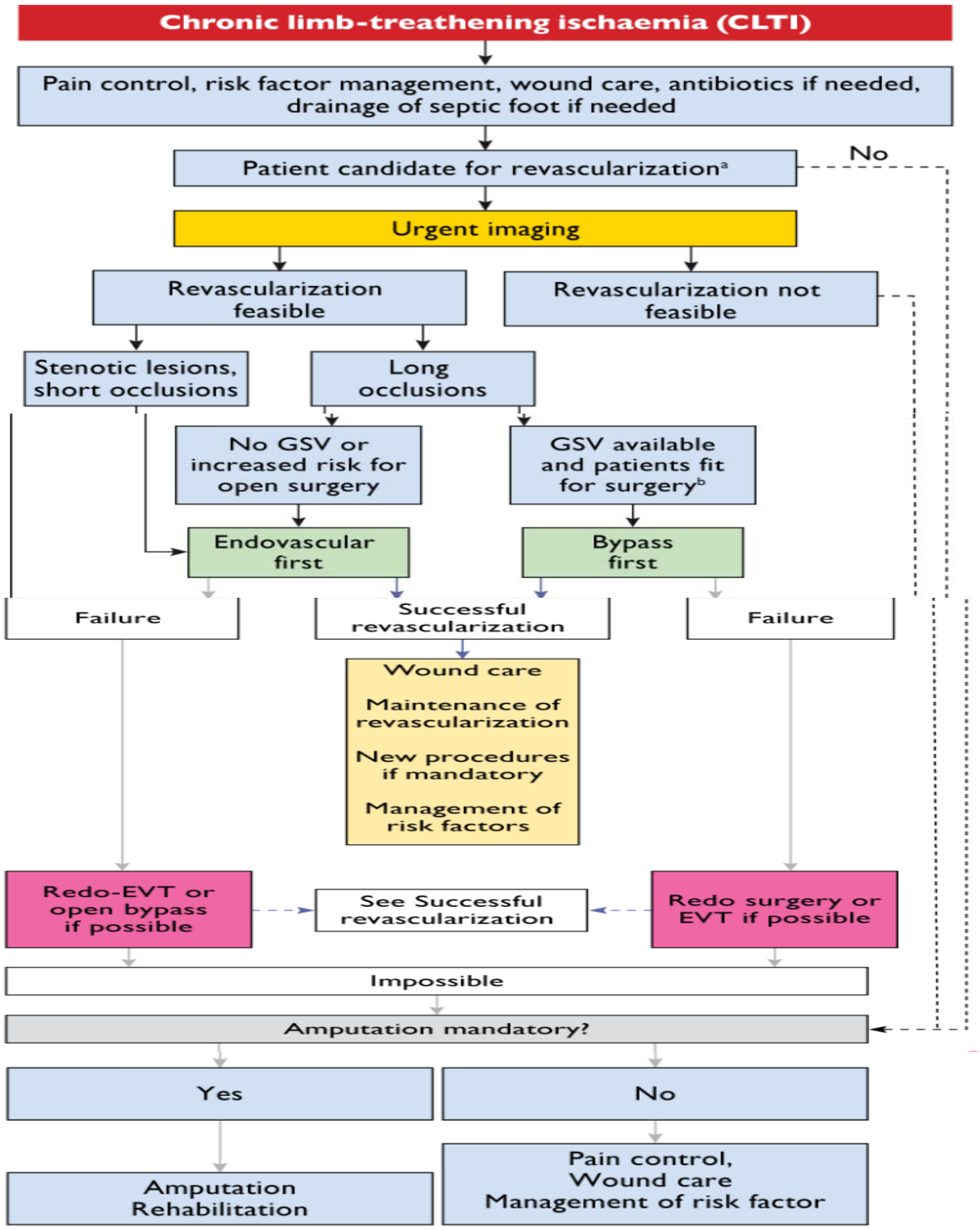
ABI = ankle-brachial index;TcPO2 = transcutaneous oxygen pressure.

Figure 8 Estimation of the amputation risk according to the WIfI classification (see also Table 7)[a]

Estimate risk of amputation at I year for each combination				
	Ischaemia-0			
W-0	VL	VL	L	M
W-1	VL	VL	L	M
W-2	L	L	M	H
W-3	M	M	H	H
	fI-0	fI-1	fI-2	fI-3
	Ischaemia-1			
W-0	VL	L	M	H
W-1	VL	L	M	H
W-2	M	M	H	H
W-3	H	H	H	H
	fI-0	fI-1	fI-2	fI-3
	Ischaemia-2			
W-0	L	L	M	M
W-1	L	M	H	H
W-2	M	H	H	H
W-3	H	H	H	H
	fI-0	fI-1	fI-2	fI-3
	Ischaemia-3			
W-3	L	M	M	H
W-3	M	M	H	H
W-3	H	H	H	H
W-3	H	H	H	H
	fI-0	fI-1	fI-2	fI-3

fI = foot infection; H = high-risk; L = low-risk; M = moderate risk;VL = very low risk;W = wound.

Figure 9 Management of patients with chronic limb-threatening ischaemia



EVT= endovascular therapy;
GSV = great saphenous vein.
[a]In bedridden, demented and/or frail patients, primary amputation should be considered.
[b]In the absence of contra-indication for surgery and in the presence of adequate target for anastomosis/runoff.

Recommendations on the management of chronic limb-threatening ischaemia		
Recommendations	**Class[a]**	**Level[b]**
Early recognition of tissue loss and/or infection and referral to the vascular team is mandatory to improve limb salvage.	I	C
In patients with CLTI, assessment of the risk of amputation is indicated.	I	C
In patients with CLTI and diabetes, optimal glycaemic control is recommended.	I	C
For limb salvage, revascularization is indicated whenever feasible.	I	B
In CLTI patients with below-the-knee lesions, angiography including foot runoff should be considered prior to revascularization.	IIa	C
In patients with CLTI, stem cell/gene therapy is not indicated.	III	B

CLTI = chroniclimb threatening ischaemia·

Acute limb ischaemia

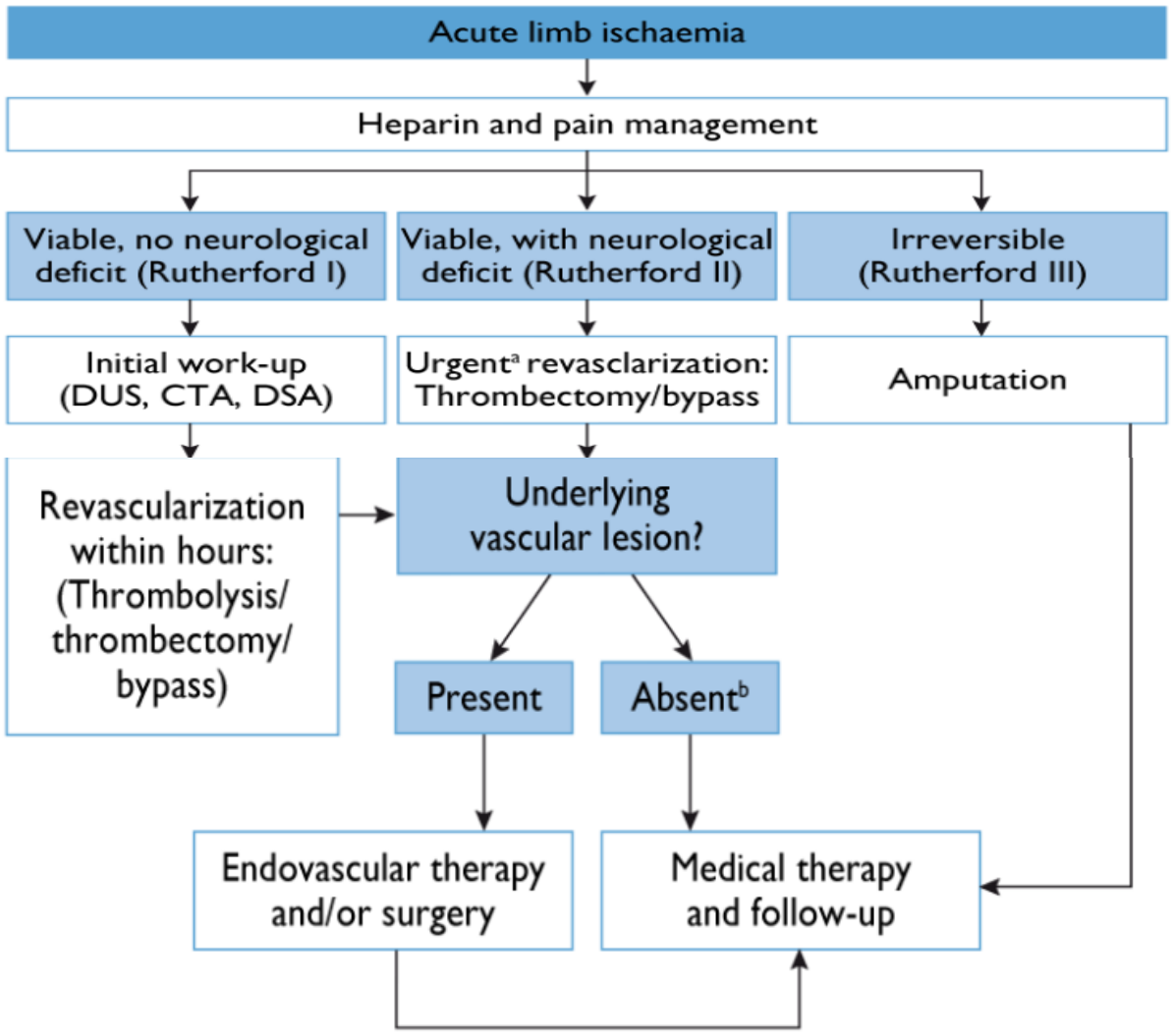
Acute limb ischaemia with neurological deficit mandates urgent revascularization.

Table 10 Clinical categories of acute limb ischaemia	
Grade I	
Category	Viable
Sensory loss	None
Motor deficit	None
Prognosis	No immediate threat
Grade IIA	
Category	Marginally threatened
Sensory loss	None or minimal (toes)
Motor deficit	None
Prognosis	Salvageable if promptly treated
Grade IIB	
Category	Immediately threatened
Sensory loss	More than toes
Motor deficit	Mild/moderate
Prognosis	Salvageable if promptly revascularized
Grade III	
Category	Irreversible
Sensory loss	Profound, anaesthetic
Motor deficit	Profound, paralysis (rigor)
Prognosis	Major tissue loss, permanent nerve damage inevitable

Recommendations for the management of patients presenting with acute limb ischaemia		
Recommendations	**Class[a]**	**Level[b]**
In the case of neurological deficit, urgent revascularization is indicated.[c]	I	C
In the absence of neurological deficit, revascularization is indicated within hours after initial imaging in a case to case decision.	I	C
Heparin and analgesics are indicated as soon as possible.	I	C

[a]Class of recommendation - [b]Level of evidence - [c]In this case imaging should not delay intervention.

Figure 10 Management of acute limb ischaemia

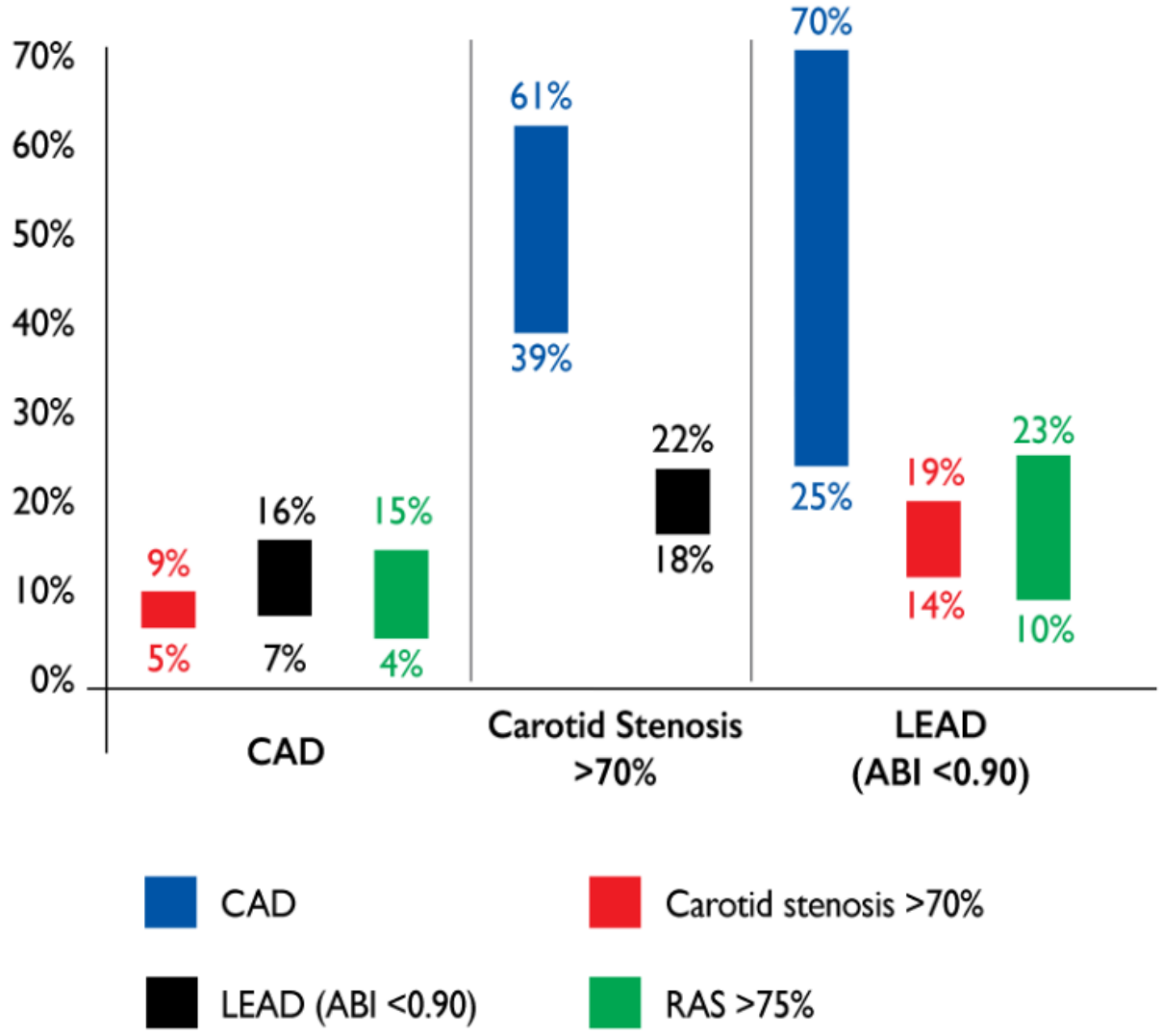


CTA = computed tomography angiography; DSA = digital subtraction ultrasound; DUS = duplex ultrasound.

[a]Imaging should not delay revascularization - [b] Specific etiological work-up is necessary (cardiac, aorta).

Multisite artery disease (MSAD) is defined by the simultaneous presence of clinically relevant atherosclerotic lesions in at least two major vascular territories ranging from 10–15% in patients with CAD to 60–70% in patients with severe carotid stenosis or LEAD (Figure 12).

Figure 11 Reported rate ranges of other localizations of atherosclerosis in patients with a specific arterial disease



The graph reports the rates of concomitant arterial diseases in patients presenting an arterial disease in one territory (e.g. in patients with CAD, 5–9% of cases have concomitant carotid stenosis >70%).

ABI = ankle-brachial index; CAD = coronary artery disease; LEAD = lower extremity artery disease; RAS = renal artery stenosis.

MSAD is invariably associated with worse clinical outcomes; however, systematic screening for asymptomatic disease in additional vascular sites has not been proven to improve prognosis and is yet not indicated. In patients with any presentation of PADs, clinical assessment of symptoms and physical signs of other localizations and/or CAD is necessary, and in case of clinical suspicion, further tests may be planned. Screening for asymptomatic lesions may be interesting in some cases (Table 11). This is the case for patients undergoing CABG, where ABI measurement may be considered especially when saphenous vein harvesting is planned, and carotid screening should be considered in a subset of patients at high risk of carotid artery disease.

Table 11 Indication for screening of associated atherosclerotic disease in additional vascular territories

Landing disease \ Screened disease	CAD	LEAD	Carotid	Renal
CAD				
Scheduled for CABG		IIa[a]	IIb[c] / I[b]	U
Not scheduled for CABG		IIb	NR	U
LEAD				
Scheduled for CABG	I[d]		NR	U
Not scheduled for CABG	NR		NR	U
Carotid stenosis				
Scheduled for CEA/CAS	IIb	NR		U
Not scheduled for CEA/CAS	NR	NR		U

CABG = coronary artery bypass grafting; CAD = coronary artery disease; CAS = coronary endarterectomy; CKD = chronic kidney disease; ECG = electrocardiogram; LEAD = lower extremity artery disease; NR = no recommendation (not enough evidence to support systematic screening); TIA = transient ischaemic attack; U = uncertain.

[a]Especially when venous harvesting is planned for bypass - [b]In patients with symptomatic cerebrovascular disease.

[c]In patients with asymptomatic carotid disease and: age ≥ 70 years, multivessel CAD, associated LEAD or carotid bruit. [d]Screening with ECG is recommended in all patients and with imaging stress testing in patients with poor functional capacity and more than two of the following: history of CAD, heart failure, stroke or TIA, CKD, diabetes mellitus requiring insulin therapy.

Recommendations on screening for carotid disease in patients undergoing coronary artery bypass grafting

Recommendations	Class[a]	Level[b]
In patients undergoing CABG, DUS is recommended in patients with a recent (<6 months) history of TIA/stroke.	I	B
In patients with no recent (< 6 months) history of TIA/stroke, DUS may be considered in the following cases: age ≥70 years, multivessel coronary artery disease, concomitant LEAD, or carotid bruit.	IIb	B
Screening for carotid stenosis is not indicated in patients requiring urgent CABG with no recent stroke/TIA.	III	C

CABG = coronary artery bypass grafting; DUS = duplex ultrasound; LEAD = lower extremity artery disease; TIA = transient ischaemic attack.
[a]Class of recommendation - [b]Level of evidence.

Recommendations on the management of carotid stenosis in patients undergoing coronary artery bypass grafting

Recommendations	Class[a]	Level[b]
It is recommended that the indication (and if so the method and timing) for carotid revascularization be individualized after discussion within a multidisciplinary team, including a neurologist.	I	C
In patients scheduled for CABG, with recent (<6 months) history of TIA/stroke:		
• Carotid revascularization should be considered in patients with 50–99% carotid stenosis.	IIa	B
• Carotid revascularization with CEA should be considered as first choice in patients with 50–99% carotid stenosis.	IIa	B
• Carotid revascularization is not recommended in patients with carotid stenosis <50%.	III	C
In neurologically asymptomatic patients scheduled for CABG:		
• Routine prophylactic carotid revascularization in patients with a 70–99% carotid stenosis is not recommended.	III	B
• Carotid revascularization may be considered in patients with bilateral 70–99% carotid stenoses or 70–99% carotid stenosis + contralateral occlusion.	IIb	B
• Carotid revascularization may be considered in patients with a 70–99% carotid stenosis, in the presence of one or more characteristics that may be associated with an increased risk of ipsilateral stroke, [c] in order to reduce stroke risk beyond the perioperative period.	IIb	C

CABG = coronary artery bypass grafting; CAS = carotid artery stenting; CEA = carotid endarterectomy

Recommendations for screening and management of concomitant lower extremity artery disease and coronary artery disease		
Recommendations	**Class[a]**	**Level[b]**
In patients with LEAD, radial artery access is recommended as the first option for coronary angiography/intervention.	I	C
In patients with LEAD undergoing CABG, sparing the autologous great saphenous vein for potential future use for surgical peripheral revascularization should be considered.	IIa	C
In patients undergoing CABG and requiring saphenous vein harvesting, screening for LEAD should be considered.	IIa	C
In patients with CAD, screening for LEAD by ABI measurement may be considered for risk stratification.	IIb	B

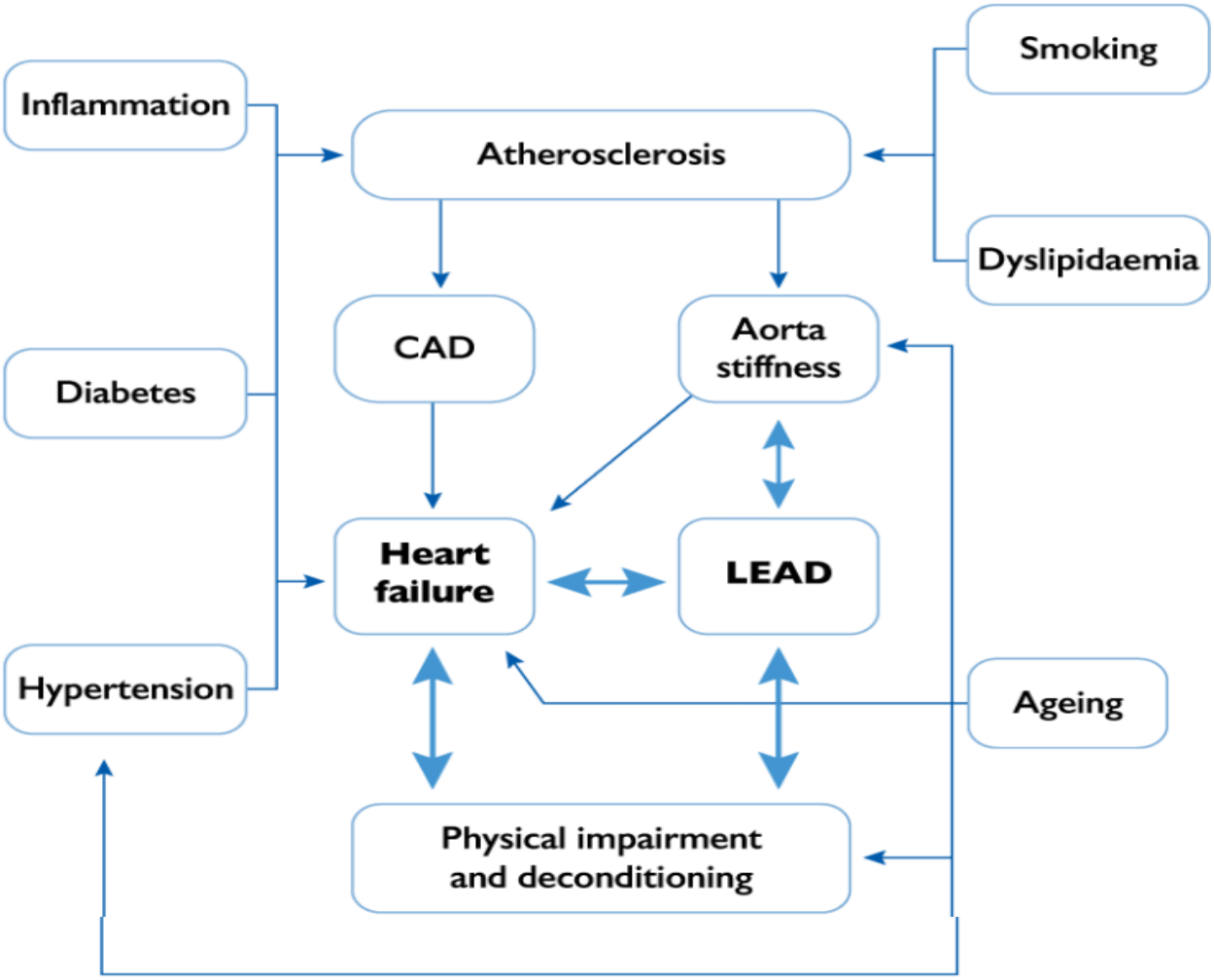
ABI = ankle-brachial index; CABG = coronary artery bypass grafting; CAD = coronary artery disease; LEAD = lower extremity artery disease;TIA = transient ischaemic attack.

[a]Class of recommendation - [b]Level of evidence.

Recommendation on screening for coronary artery disease in patients with carotid disease		
Recommendations	**Class[a]**	**Level[b]**
In patients undergoing elective CEA, preoperative CAD screening, including coronary angiography, may be considered.	IIb	B

Cardiac conditions other than CAD are frequent in patients with PADs. This is especially the case for heart failure and atrial fibrillation in patients with LEAD.

Figure 12 Interrelations between heart failure and lower extremity artery disease



Recommendations on the management of heart failure associated with PADs

Recommendations	Class[a]	Level[b]
Full vascular assessment is indicated in all patients considered for heart transplantation or cardiac assist device implantation.	I	C
In patients with symptomatic PADs, screening for heart failure with TTE and/or natriuretic peptides assessment should be considered.	IIa	C
Screening for LEAD may be considered in patients with heart failure.	IIb	C
Testing for renal artery disease may be considered in patients with flash pulmonary oedema.	IIb	C

LEAD = lower extremity artery disease;TTE = transthoracic echocardiography; PADs = peripheral arterial diseases

Recommendations on the management of atrial fibrillation associated with PADs

Recommendations	Class[a]	Level[b]
In patients with LEAD and atrial fibrillation, oral anticoagulation:		
• is recommended when CHA_2DS_2-VASc score ≥2	I	A
• should be considered in all other patients.	IIa	B

LEAD = lower extremity artery disease; PADs = peripheral arterial diseases; CHA2DS2VASC = Congestive heart failure; Hypertension; Age ≥75 years; Diabetes mellitus; prior Stroke or TIA; Vascular disease; Age 65–74 years; Sex Category female.

Recommendations on the management of valvular heart disease associated with PADs

Recommendations	Class[a]	Level[b]
Screening for LEAD and UEAD is indicated in patients undergoing TAVI or other structural interventions requiring an arterial approach.	I	C

LEAD = lower extremity artery disease; PADs = peripheral arterial diseases; TAVI = transcatheter aortic valve implantation; UEAD = upper extremity artery disease.